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EXAMINER	
LIU, SUE XU	

ART UNIT	PAPER NUMBER
1639	

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12/07/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/084,892	CHAKRAVARTI, SHUKTI	
	Examiner	Art Unit	
	SUE LIU	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56-59,61 and 64-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56-59,61 and 64-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/22/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

1. Claims 1-55, 60, 62 and 63 have been canceled as filed on 9/9/09.

Claims 56-59, 61 and 64-68 are currently pending.

Claims 56-59, 61 and 64-68 are being examined in this application.

Election/Restrictions

2. Applicant's election with traverse of the following species:

A.) GRO1 (SEQ ID NO:2)

in the reply filed on 9/24/08 is previously acknowledged. Applicants have amended the claims encompass both GRO1 and SLC26A2 genes. Thus, claim 58 is rejoined and examined.

Priority

3. This application is a CIP of 09/694,758 (filed on 10/23/2000), which claims priority to provisional applications 60/160,835 (filed on 10/21/1999).

Information Disclosure Statement

4. The IDS filed on 5/22/09 has been considered except where the references are crossed out due to either no date information or no copy was provided. See the attached PTO 1449 form.

Claim Objection(s) / Rejection(s) Withdrawn

5. All previous claim Objection(s) / Rejection(s) as set forth in the previous Office action (mailed 12/22/08) that are not repeated and/or maintained in the instant Office action are withdrawn due to applicant's amendments to the claims.

New Claim Objection(s) / Rejection(s)

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 56-59, 61 and 64-68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is necessitated by applicant's amendments to the claims.

Claim 56 recites "an array" comprising probes for both GRO1 and SLC26A2 genes, but the said claim also recites probes are complementary to "GRO1 or SLC26A2". In other words, the claim recites probes for both gene are encompassed, but also recites either one of the two genes is required. Thus, it is not clear what probes are comprised by the claimed array.

Claim 61 recites "said nucleic acid probe**s** consist of **a** sequence that is…" which statement is confusion. It is not clear if all of the "probes" (i.e. a plurality of probes) have the "one" of the same sequence or each one of the probes has a sequence. Further, claim 61 also

recites "said nucleic acid probes…that is complementary to… SEQ ID NO:2 **or** SEQ ID NO:176", which seems to recite that only one of the alternative genes (GRO1 or SLC26A2) is encompassed by the claims and thus conflicting with the "and" in claim 56.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Heller and Others

9. Claims **56-59**, **61** and **64-68** are rejected under 35 U.S.C. 103(a) as being unpatentable over **Heller** et al (PNAS. Vol.94: 2150-2155; 1997; cited previously), in view of **Lockhart** et al (Nature Biotechnology. Vol.14: 1675-1680; 1996; cited in IDS) and **GenBank** accession Number U14528 (Downloaded from ncbi.nlm.nih.gov; downloaded on 12/4/09) as well as Hastbacka et al. (Cell. Vol.78(6): 1073-1087; 1993). This rejection is necessitated by applicant's amendments to the claims.

Heller et al, The instant claims recite "An array to aid in diagnosing ulcerative colitis (UC) in a subject comprising:

(a) nucleic acid probes for determining an expression level of a melanoma growth stimulatory activity (GRO1) gene product (SEQ ID NO:2) and a SLC26A2 gene product (SEQ ID NO:176) in a sample from said subject; and

(b) a substrate to which said nucleic acid probe are bound, wherein said nucleic acid probes are 12-40 nucleotides in length, complementary to said GRO1 or SLC26A2 genen product, and hybridize under high stringency conditions to said GRO1 or SLC26A2 gene product, and

wherein an increase in the expression level of said GRO1 gene product or a decrease in the expression level of said SLC26A2 gene product in said sample relative to the expression level of the same gene product in normal tissue indicates that said subject has UC."

The above underlined regions of the instant claim 56 are recitations of intended uses of the instant claimed product of "an array".

Heller et al, throughout the publication, teach using microarray to detect various gene expression including the expression of GRO 1(or GRO α) (e.g. Abstract), which the microarray reads on the array of **clm 56**. Heller et al disclose a 96 gene micro array design (i.e., see the results section, page 2151 and fig.1) and 1046 element array. The reference micro-array comprises probes from following genes Il-6, Il-8, GH1, Gro1, MIP, stromelysin 1, which the probes of Gro1 reads on the nucleic acid probes of **clm 56**. The reference also teaches immobilizing the nucleic acid probes to glass slides (e.g. p.2150, left col.), which the glass slide read on the substrate of **clms 56** and **64**. The reference also teaches the cDNA for the various genes are sequenced and compared to known database (e.g. p.2154).

As discussed above, the underlined regions of **clm 56** as well as the recitations of **clms 57** and **59** are recitations of intended uses.

A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

The reference teaches the microarray containing probes for Gro1 gene can be used to monitor the expression level of Gro1 gene, and thus demonstrating the microarray of the reference is capable of performing the intended use.

The reference also teaches printing the probes onto the glass slide (e.g. p.2150, left col.), which inherently requires covalent or hydrophobic interaction between the probes and the substrate as recited in **clm 65**.

The microarray of the reference is a two dimensional array as indicated in Figure 2 of the reference, which reads on the array of **clm 66**.

The reference also teaches fluorescently labeling probes (e.g. p.2153, right col.), which read on the labeling of **clms 67** and **68**.

Heller et al, do not explicitly teach using short nucleic acid as probes to generate the nucleic acid array as recited in **clms 56** and **61**. The reference also does not explicitly teach the array to have probes that are complementary to the SLC26A2 gene as recited in **clms 56** and **58**.

However, **Lockhart** et al, throughout the publication, teach making microarrays comprising oligonucleotides (short nucleic acids) (e.g. Abstract). The reference teaches covalently attach 20-mer oligonucleotides to solid support (e.g. p.1676), which read on the nucleotide length of **clms 60** and **61**. The reference also teaches the designing oligonucleotide

probes that are complementary (based on sequence information) to the genes of interest (e.g. p.1676, right; Figure 5). The reference also teaches the advantages of generating such arrays so that simultaneous monitoring of tens of thousands of genes can be carried out (e.g. Abstract) as well as providing improved resolution (e.g. p.1676). The reference also teaches the need to develop arrays comprising probes for tens of thousands of human genes so that parallel experiments on these different genes can be conducted (e.g. Abstract).

Further, the sequence for SLC26A2 gene with GenBank accession number U14528 is known in the art. The publication (Hastbacka et al.) that discloses the said GenBank accession number discloses the SLC26A2 or the sulfate transporter (or DTDST) plays an important role in human physiology such as its role in various diseases.

Therefore, it would have been prima facie obvious at the time the invention was made for a person of ordinary skill in the art to generate an array with oligonucleotide probes that are complementary to various genes including GRO1 and SLC26A2 genes with short length.

A person of ordinary skill in the art would have been motivated at the time of the invention to include probes for various genes including SLC26A2, because Lockhart teaches the need and advantages of generating arrays having various numbers of probes for tens of thousands of genes so that the gene expression pattern can be monitored simultaneously. In addition, the SLC26A2 gene has been shown to be an important gene for various diseases. Thus, one of skill in the art would have been motivated to include probes for the SLC26A2 gene in an array especially the one for global gene expression analysis. Thus, it would have been obvious to one of ordinary skill in the art to apply the standard technique of generating probes for any gene of

interest and include the probes in an array as taught by Lockhart, to improve the microarray for the predicable result of enabling standard gene expression monitoring.

A person of ordinary skill in the art would have been motivated at the time of the invention to design a microarray comprising short oligonucocotide probes (such as 20-mers) for the GRO1 gene, because Lockhart et al teach the advantages of using short oligonucleotide as probes to provide increased resolution and efficient hybridization assays. In addition, because both the cited references teach DNA microarrays comprising various probes, it would have been obvious to one skilled in the art to substitute one type of probes (cDNA probes) for the other (oligonucleotide probes) to achieve the predictable result of making a DNA microarray for measuring the expression of genes of interest.

An ordinary skilled artisan would have reasonable expectation of success of achieving such modifications since the method of generating a microarray with specific nucleic acid probes are know in the art such as the one taught by the above cited references.

Dieckgraefe and Heller

10. Claims **56-59, 61** and **64-68** are rejected under 35 U.S.C. 103(a) as being unpatentable over **Dieckgraefe** et al (Gastroenterology, vol. 114, no. 4, G3954; April, 1998; cited in IDS 8/12/2002), in view of **Heller** et al (PNAS. Vol.94: 2150-2155; 1997; cited previously), and **GenBank** accession Number U14528 (Downloaded from ncbi.nlm.nih.gov; downloaded on 12/4/09) as well as Hastbacka et al. (Cell. Vol.78(6): 1073-1087; 1993). This rejection is necessitated by applicant's amendments to the claims.

Dieckgraefe et al, throughout the publication, disclose characterization of mucosal gene expression in inflammatory bowel disease (IBD) by direct hybridization to massive parallel oligonucleotide arrays (see the entire document), which reads on the array of **clms 56** as well as the substrate of **clm 64** and **66**. The reference discloses that parallel or high throughput methods of measuring gene expression have been recently developed which allow concurrent measurement of the expression pattern of a large number of genes. The reference discloses the use of Gene chip (refers to the solid support chip and two dimensional matrix of the instant claims) expression monitoring system to examine mucosal gene expression in ulcerative colitis, Crohn's colitis to identify genotypes associated with particular disease. The reference discloses that RNA isolated from the mucosal colonial specimens was used to generate hybridization probes. This reads on the intended use of **clms 56, 57**, and **59**. The reference further discloses that light directed solid phase (refers to the support of the instant claims of **clm 56**) combinatorial chemistry (would refer to covalent bonding of probes to the substrate of **clm 65**) was used to generate oligonucleotide probe arrays (refers to nucleic acid probes of the instant claim array) which provide representation of nearly 7000 human cDNA and EST sequences, which reads on the probes specifically hybridize to the gene products of **clm 56**. The reference also teaches using 25-mer oligos, which reads on the length of **clms 60** and **61**. The reference further discloses that hybridization to the oligonucleotide arrays was sensitive, specific and reproducible.

Dieckgraefe et al do not specifically teach probes for GRO1 gene as recited in **clms 56** and **58** as well as labeling the nucleic acid probes as recited in **clms 67** and **68**.

However, **Heller** et al, throughout the publication, teach using microarray to detect various gene expression including the expression of GRO 1(or GRO α), as discussed supra. The reference also teaches fluorescently labeling probes (e.g. p.2153, right col.).

Further, the sequence for SLC26A2 gene with GenBank accession number U14528 is known in the art. The publication (Hastbacka et al.) that discloses the said GenBank accession number discloses the SLC26A2 or the sulfate transporter (or DTDST) plays an important role in human physiology such as its role in various diseases.

Therefore, it would have been prima facie obvious at the time the invention was made for a person of ordinary skill in the art to generate an array with oligonucleotide probes that are complementary to various genes including GRO1 and SLC26A2 genes.

A person of ordinary skill in the art would have been motivated at the time of the invention to include probes for various genes including SLC26A2, because Dieckgraefe teaches the need and advantages of using "massively parallel" oligonucleotide arrays having various numbers of probes thousands of human genes. In addition, the SLC26A2 gene has been shown to be an important gene for various diseases. Thus, one of skill in the art would have been motivated to include probes for the SLC26A2 gene in an array especially the one for global gene expression analysis. Thus, it would have been obvious to one of ordinary skill in the art to apply the standard technique of generating probes for any gene of interest and include the probes in an array as taught by Dieckgraefe, to improve the microarray for the predicable result of enabling standard gene expression monitoring. In addition, it is highly likely that the 260,000 indivdual 25-mer oligonucleotides on the GeneChip array system would comprise probes that are

complementary to GRO1 and SLC26A2 genes without evidence to the contrary, since the probes represent nearly 7000 human genes.

A person of ordinary skill in the art would have been motivated at the time of the invention to design a microarray comprising probes for the GRO1 gene, because Heller et al teach that the need to monitor genes (such as GRO1) that are associated with inflammation. In addition, because both the cited references teach DNA microarrays comprising various probes for various genes, it would have been obvious to one skilled in the art to substitute one gene probe for the other to achieve the predictable result of making a DNA microarray for measuring the expression of genes of interest.

An ordinary skilled artisan would have reasonable expectation of success of achieving such modifications since the method of generating a microarray with specific nucleic acid probes are know in the art such as the one taught by Diechkgraefe et al and the specific gene sequence for the desired marker is also know as taught by Heller et al.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUE LIU whose telephone number is (571)272-5539. The examiner can normally be reached on 9am-4pmpm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached at 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SUE LIU/
Patent Examiner, Art Unit 1639
12/4/09